Computational and spectroscopic investigation of 7-azaindole: Solvation and intermolecular interactions

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Abstract

We report results of an experimental and computational study of 7-azaindole (7AI). This system has been studied extensively due to its role as a simplified model for hydrogen bonding interactions in DNA base pairs. In this study we use laser resonance Raman spectroscopy to investigate excited state dynamics of 7AI and its dimer. We selectively probe the monomer and dimer by varying concentration and excitation wavelengths. The trend in stability of the dimer is quantified in various solvents using ab initio and DFT calculations with implicit and explicit solvation models.
Overview

- Project background
- Resonance Raman spectroscopy primer
- Computational theory
- Computational results with interpretation
- Experimental and simulated spectral overlay
- Conclusions
- Future work
It has been well established that 7AI readily forms H-bonded dimers in solution\(^1\).

In a formal sense, the N---H-N bonds contained in the 7AI dimer are nearly identical to the ones in the adenine-thymine base pairs.

Another similarity between 7AI and DNA base pairs is that these systems all have higher than expected Gibbs energies of association\(^2\) indicating that there are other significant factors that contribute to the great stability of these systems.

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7-azaindole dimer
Computational Overview

- 7-azaindole energetics and solvation
  - dimer geometry
  - Enthalpy and Gibbs energy of association
- Resonance Raman spectral simulation
  - Correlate with experiment
  - Excited state double proton transfer?
7-azaindole dimer geometry
B3LYP/6-31G(d) CPCM
## Gas Phase Results

**HF/6-31G(d)**

**B3LYP/6-31G(d)**

<table>
<thead>
<tr>
<th>Species</th>
<th>H (kJ/mole)</th>
<th>G (kJ/mole)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monomer</td>
<td>-377.3349</td>
<td>-379.7353</td>
</tr>
<tr>
<td>Dimer</td>
<td>-754.6858</td>
<td>-759.4954</td>
</tr>
<tr>
<td>Monomer w/2 Explicit</td>
<td>-529.3293</td>
<td>-532.5450</td>
</tr>
<tr>
<td>2H₂O</td>
<td>-151.9670</td>
<td>-152.7667</td>
</tr>
<tr>
<td>dimer-2 monomer</td>
<td>-42.1</td>
<td>-65.0</td>
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<tr>
<td>monomer w/2 H₂O - 2H₂O</td>
<td>-71.8</td>
<td>-112.9</td>
</tr>
<tr>
<td>experimental¹</td>
<td>-39.7</td>
<td></td>
</tr>
</tbody>
</table>

Continuum Solvation

HF/6-31G(d) PCM
B3LYP/6-31G(d) PCM

<table>
<thead>
<tr>
<th>Species</th>
<th>Gas Phase</th>
<th></th>
<th></th>
<th>Continuum Solvation</th>
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<tr>
<td></td>
<td></td>
<td>H</td>
<td>G</td>
<td>H</td>
<td>G</td>
<td></td>
</tr>
<tr>
<td>Dimer</td>
<td>-754.6858</td>
<td>-759.4954</td>
<td>-754.7424</td>
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<td>2H2O</td>
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<td>dimer-2 monomer</td>
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<td>1.1</td>
<td>-19.3</td>
<td>6.2</td>
<td>46.9</td>
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<tr>
<td>monomer w/2 H2O - 2H2O</td>
<td>-71.8</td>
<td>-112.9</td>
<td>13.1</td>
<td>-55.6</td>
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<td>53.8</td>
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<td>experimental1</td>
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</tbody>
</table>

-42.1 -65.0 1.1 -19.3 6.2 46.9 47.7 91.7

Correction for basis set superposition error

- Fragments are able to utilize basis functions on other fragments providing a different description of the system than in the monomer \(\Rightarrow\) error in energy of association

- To study energetics of A+B \(\rightarrow\) AB cluster

\[
\text{Association Energy}_{AB}^{cc}(G) = E_{AB}(G,AB) - E_A(G,AB) - E_B(G,AB)
\]

Where \(E_{AB}(G,AB)\) is AB energy at geometry of cluster and \(E_A(G,AB)\) and \(E_B(G,AB)\) are the energies of each fragment individually with “ghost” atoms in place of other fragment at cluster geometry.
**Counterpoise corrected results**

<table>
<thead>
<tr>
<th>Species</th>
<th>gas phase</th>
<th>solvated</th>
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</thead>
<tbody>
<tr>
<td>dimer</td>
<td>-759.7614605</td>
<td>-759.744052</td>
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<tr>
<td>A</td>
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<td>-379.853668</td>
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<tr>
<td>B</td>
<td>-379.87108</td>
<td>-379.853671</td>
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<td>-0.036713</td>
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<tr>
<td>kJ/mole</td>
<td>-50.7</td>
<td>-96.4</td>
</tr>
</tbody>
</table>

- Solvated results utilize PCM model and may not correctly reflect ghost atom properties
Laser Raman Spectroscopy

Raman

Resonance Raman

Virtual Level

Laser

Rayleigh

Raman

Ground State

Resonance enhancement:
1. $\sim 10^5$
2. Chromophore selective
3. Sensitive to local structure
Computational Theory

Resonance Raman Intensity Calculation
Short time wave-packet propagation approximation

Intensity of the $k^{th}$ vibrational band:

$$ I_k \propto \omega_L (\omega_L - \omega_k)^3 \Delta_k^2 \omega_k^2 $$

$$ I_k \propto \omega_L (\omega_L - \omega_k)^3 \Delta_k^2 |\Phi(\omega_L) - \Phi(\omega_L - \omega_k)|^2 $$

+ scaled quantum mechanical force constants (SQM)
→ ~15 cm$^{-1}$ vibrational frequency accuracy

Resonance Raman spectral Simulation:

Three Computational Steps:

1.) Ground State: B3LYP/6-31G(d) frequency and optimization.

2.) Excited State (resonant state): CIS/6-31G(d) frequency using the optimized geometry from calculation #1.

3.) HF/6-31G(d) frequency to correct the gradient predicted in calculation #1.

The vibrational modes are then scaled by Quantum mechanical force constants based on internal coordinates.
Web Interface for Spectral Simulation

Three steps:

1. Select Gaussian ground state frequency log file to upload:
   [BROWSE...]

2. Scale frequencies only [no RR simulation, only file (required)]
   [No Scaling]

3. Select Gaussian excited state gradient calculation log file to upload:
   [BROWSE...]

Gustavus Resonance Raman Spectral Simulator

Excitation wavelength (nm)
532.0

Simulated spectral width [cm-1]
30.0

+ or - HF gradient
-1

Import Gaussian log

Created by Jonathan Smith
updated: January 23, 2006
Resonance Raman of 7Al: Experiment Meets Theory

Concentration: 0.0033M
Solvent: Methanol
Wavelength: 274 nm
Conclusions

The calculations indicate that the dimerization process of 7Al is unfavorable (positive $\Delta G$) in aqueous solution. This can be explained by a loss of favorable solvent interactions with solvent and an entropic gain balanced by favorable hydrogen bonding between 7Al monomers. Previous studies of DNA base pairs have yielded similar findings but also show that the interaction of a second base pair with the first is a favorable process (negative $\Delta G$). Less polar and non-hydrogen bonding solvents should make dimerization more favorable.

The Raman simulation of the 7Al monomer provides relatively good agreement with the experimental spectrum in methanol. However, further investigation will be required to determine whether or not the experimental spectrum shows evidence of the 7Al dimer and related excited state double proton transfer.
Future Investigations

- Further develop the Raman simulator methodology to more accurately predict Raman spectra

- To explore the dimer in the gas phase using fluorescence spectroscopy to accompany the computational gas phase calculations

- Study the solvent interactions by tuning solvent properties.
Cold Isolated Gas Phase Molecules

Molecular beam:

100 psi
He + X

Vacuum: 10^-6 Torr

Laser

- Cold molecules
- Clusters

Detection:
- Collect Fluorescence
- Time of flight mass spectrometer
Acknowledgements

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